REMARKS

The Final Office Action and the cited and applied references have been carefully reviewed. No claim is allowed. Claims 93, 99, 100, 104, 106, 107, 116, 121 and 122 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 93, 99, 100, 104, 106, 107, 116, 121 and 122 have been rejected under 35 USC §103(a) as being unpatentable over Nakamura et al (*Infect. Immun.* 61:64-70, 1993) and further in view of Campbell (*Laboratory Techniques in Biochemistry and Molecular Biology*, Volume 13, Chapter 1, pages 1-33, 1984). In response to applicants' arguments, the examiner maintains this rejection, stating that Nakamura identified the serum IGIF, demonstrated its functional activity, and purified it to a certain degree; and that the state of recombinant technology was high at the time the invention was made, and thus isolating a gene encoding a serum protein or identifying a cell source producing the protein was not unprecedented. The examiner further states that there is no evidence which show the following (see the bottom half of page 3 of the Office Action):

(1) a person of ordinary skill in the art would be able to identify the cell producing the IGIF or the gene encoding the IGIF based on the teachings of Nakamura and readily available techniques in the relevant field in the absence (of evidence) to the contrary;

(2) either Nakamura or others in the field had tried and failed repeatedly to identify the cell producing the IGIF or the gene encoding IGIF; and

(3) if persons skilled in the art who were presumably working on the problem knew of the teachings of the above cited references, they would still be unable to solve the problem.

This rejection is respectfully traversed.

Applicants respectfully disagree with the examiner for the following reasons:

With Respect To Issue (1) Above

Nakamura clearly states at page 69, left column, top of second paragraph:

> *The cells producing the factor have also not been identified*. In order to get enough factor for a detailed analysis of its molecular characteristics, this problem of identification should be solved. (emphasis added)

As is evident from the above statement, Nakamura clearly states that the cells producing the factor had not yet been identified at the time Nakamura was published. Under the circumstance, it is also clear that the **source** of the gene encoding IGIF was unknown. Therefore, it would be impossible even for a skilled person to identify the gene without prior knowledge about the **source** of the gene.

Applicants therefore believe that the cited and applied Nakamura reference *per se* provides the evidence for the issue (1) pointed out by the examiner.

With Respect To Issue (2) Above

The evidence which the examiner appears to require is what would be considered as so called "negative" data. As would

be readily recognized by those of ordinary skill in the art, it is difficult to submit publications which show such negative data, because negative data is not normally published. Nevertheless, the examiner's attention is invited to the following statement made in Okamura (*Infection and Immunity*, Vol.63, No.10, pp.3966-3972, 1995), which was previously cited and relied upon by the examiner:

> *Since it was difficult to get enough of the factor from serum to analyze, liver extracts were examined.* A marked costimulatory activity for IFN-gamma induction in T cell was observed in the liver extracts... (emphasis added)

Please note that Okamura was published in 1995, two years later than Nakamura. Therefore, the above statement in Okamura means that Okamura at last succeeded in identifying IGIF producing cells two years after Nakamura's publication. Since it is considered that either Nakamura or others in the field have tried to identify the cell producing the IGIF or the gene encoding IGIF after Nakamura was first published, the fact that Okamura only identified the producing cells two years later is indirect circumstantial evidence that Nakamura or others had repeatedly failed to identify the cells that produce IGIF or the gene encoding IGIF during that two year period.

With Respect To Issue (3)

Nakamura and Campbell are published prior art documents, and therefore it is presumed that one of skill in the art would know the teachings of these references. Campbell states as follows:

> *In theory*, monoclonal antibody production does not require a pure antigen since the

> appropriate antibody is selected from the cloned culture. (emphasis added)
>
> Consequently while *it may be true in general* to say that no purification procedures are required, *this may not be true in practice* with any specific antigenic mixture. (emphasis added)

It is clear from Campbell's teaching above that it would be difficult *in practice* to obtain a monoclonal antibody without a purified antigen.

As discussed above, the evidence required by the examiner is indeed provided by Nakamura, Campbell and Okamura, and the state of the art in the relevant field.

Accordingly, the evidence discussed above does indeed support Dr. Okamura's Declaration Under §1.132 filed with the Amendment of September 24, 2009. The combination of Nakamura and Campbell does not make obvious the presently claimed invention.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

In view of the above, the claims define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

If the examiner has any questions or suggestions, she is respectfully invited and requested to contact the undersigned at (202) 628-5197.

Respectfully submitted,

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